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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/896,324 | 06/29/2001 | Bi-Yu Li | TM0011-UT | 8386 |

29748 7590 09/30/2004

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EXAMINER

CHUNDURU, SURYAPRABHA

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1637

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|---|----------------------------------|--|
| Office Action Summary | Application No. 09/896,324 | Applicant(s) LI ET AL. | |
| | Examiner Suryaprabha Chunduru | Art Unit 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' response to the office action filed on July 12, 2004 has been entered.
2. The instant application is filed on June 29, 2001, which claims priority to a provisional application No. 60/215,596, filed on June 30, 2000.
3. Claims 1-8 are pending. Claims 9-23 are cancelled.

Response to arguments

4. Applicants' response to the office action is fully considered and found persuasive in part.
5. With reference to the arguments regarding obviousness rejection made in the office action of May 21, 2003, of claims 1-13, and 15-21, examiner herewith confirms the withdrawal of the rejection.
6. The following is the rejection made in the previous office action under 35 USC 102(b):

Claim 1-8, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Kato (USPN.5,707,807).

Kato teaches a method of claim 1-2 and 4, for amplifying a population of polynucleotides comprising

- (a) reverse transcribing an RNA population to provide a double-stranded population (see column 4, lines 11-12);
- (b) digesting said cDNA population with one or more restriction endonucleases (see column 4, lines 12-35) having a degenerate recognition *or* cleavage sequence, wherein the said restriction endonuclease is a three- to eight-base cutter (see column 7, lines 19-29, which include restriction endonucleases having degenerate bases) and wherein the

degenerate recognition *or* cleavage sequence is represented by N^m where N is the extent of degeneracy (N is 2-4) and m is number of degenerate bases (m is 1-5) (restriction enzymes) produce different single stranded overhangs for each restriction endonuclease (see column 7, lines 30-35, lines 49-56, wherein cohesive ends are formed with a mixture of A, C, G, and T bases);

(c) ligating said fragments to a series of adaptors lacking restriction endonuclease sites (biotinylated adaptors having degenerate bases), wherein each adaptor is cohesive to all possible overhangs (see column 4, lines 14-21);

(d) amplifying said restriction fragments for 25 to 30 cycles which includes 25 cycles (see column 4, lines 54-61).

With regard to claim 3, Kato teaches said restriction endonuclease comprising four-base cutter (see column 7, lines 19-35);

With regard to claim 5, Kato teaches that the method uses a series of adaptors having a sequence complementary to overhangs (see column 7, lines 49-56);

With regard to claim 6, Kato teaches that said restriction fragments are amplified using PCR to produce PCR products (see column 6, lines 51-60);

With regard to claim 7, Kato teaches that said adaptors provide priming sites for PCR (see column 7, lines 66-67, column 8, lines 16);

With regard to claim 8, Kato teaches that the method comprises detection of PCR products using gel electrophoresis (see column 6, lines 57-60);

With regard to claim 15, Kato teaches that the method comprises total RNA (see column 4, lines 11-13).

Thus the disclosure of Kato meets the limitations in the instant claims.

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Response to arguments:

With regard to the above rejection, Applicants' arguments and amendment are fully considered and found not persuasive. Applicants argue that Kato et al. does not teach instant amended claim limitations that is quantifying nucleic acid molecules and thus the reference of Kato et al. does not anticipate the instant claims. These arguments are fully considered and found not persuasive because Kato et al. does teach separating and recording the amplified products using sequencer (see col. 4, line 62-65, col. 3, line 22-25). Thus Kato et al. teach quantitation of amplified nucleic acid molecules using a sequencer, which automatically records the size of the fragments based on molecular weight. Further, Kato et al. also teach the use of a primer comprising a detectable label (see col. 8, line 1-6). Thus the reference of Kato et al. meets the limitations in the instant claims and the rejection is maintained herein for claims 1-8. The rejection is withdrawn for claim 15, because of the cancellation of claim 15 by the instant amendment.

7. The following is the rejection made in the previous office action under 35 USC 102(e):

Claim 1-8, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by MacLeod et al. (USPN.6,221,600).

MacLeod et al. teach a method of claim 1-2 and 4, for amplifying a population of polynucleotides comprising

- (a) reverse transcribing an RNA population to provide a double-stranded population (see column 55, lines 11-15, lines 29-31, lines 44-45, column 5, lines 18-25);
- (b) digesting said cDNA population with one or more restriction endonucleases (see column 55, lines 11-21) having a degenerate recognition *or* cleavage sequence, wherein

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the said restriction endonuclease is a three- to eight-base cutter (see column 56, lines 37-54, which include restriction endonucleases having degenerate bases) and wherein the degenerate recognition *or* cleavage sequence is represented by N^m where N is the extent of degeneracy (N is 4-8) (see column 6, lines 1-5) and m is number of degenerate bases (m is 1-5) produce different single stranded overhangs for each restriction endonuclease (see column 19, lines 1-8, table.1, which provides restriction endonucleases consisting of degenerate bases 1-8);

(c) ligating said fragments to a series of adapters lacking restriction endonuclease sites (biotinylated adaptors having degenerate bases), wherein each adaptor is cohesive to all possible overhangs (see column 55, lines 22-23, column 33, lines 45-65);

(d) amplifying said restriction fragments (see column 55, line 24). MacLeod et al. also teach that the PCR was carried on with varying number of PCR cycles (from 24-27) and indicated exponential increase in the amount of amplifier produced for at least the 25th through the 27th cycle (see column 42, lines 50-67).

With regard to claim 2-3, MacLeod et al. teach that said restriction endonuclease comprising degenerate bases (m is 2-4) (see column 19, table.1) and four-base cutter (see column 56, lines 37-54, column 18, lines 54-65);

With regard to claim 5, MacLeod et al. teach that the method uses a series of adapters (linkers) having a sequence complementary to overhangs (see column 33, lines 45-65);

With regard to claim 6, MacLeod et al. teach that said restriction fragments are amplified using PCR to produce PCR products (see column 15, lines 65-67, column 16, lines 1-10);

With regard to claim 7, MacLeod et al. teach that said adapters provide priming sites for PCR (see column 34, lines 9-11);

With regard to claim 8, MacLeod et al. teach that the method comprises detection of PCR products (see column 6, lines 29-64);

With regard to claim 15, MacLeod et al. teach that the method comprises mRNA (see column 5, lines 19-25);

Thus the disclosure of MacLeod et al. meets the limitations in the instant claims.

Response to arguments:

With regard to the above rejection, Applicants' arguments and amendment are fully considered and found not persuasive. Applicants argue that Macleod et al. does not teach use of degenerate restriction endonucleases as claimed in the instant claims and thus does not anticipate the instant claims. These arguments are fully considered and found not persuasive because MacLeod et al. does teach the use of endonucleases having degenerate bases (see col. 19, table 1). Thus the reference of MacLeod et al. meets the limitations in the instant claims and the rejection is maintained herein for claims 1-8. The rejection is withdrawn for claim 15, because of the cancellation of claim 15 by the instant amendment.

8. with regard to the rejection made in the previous office action under 35 USC 103(a), Applicants arguments and amendment are fully considered and the rejection is withdrawn herein in view of the amendment.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

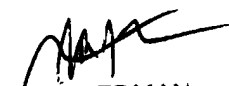
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
September 21, 2004


JEFFREY FREDMAN
PRIMARY EXAMINER
9/24/04